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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,152	TOPHAM ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *5-15,17,18,21-27,29,31,35 and 37-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,16,19,20,28,30,32-34 and 36* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/22/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-52 are pending.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-34 and 36, and the species of influenza A antigen, pulmonary lavage sample, collected 6-10 days after the antigen introduction, a human subject, and flow cytometry, in the reply filed on 08 February 2010 is acknowledged. The traversal is on the grounds that the claims all include the same corresponding technical feature of detecting the presence of or administering VLA-1$^+$ (positive) antigen-specific T cells, which constitutes a special technical feature that defines a contribution over the prior art, and that the species election should only be required when there are unreasonable numbers of species claimed. This is not found persuasive because applicants' argument did not present any issues that materially affect the rationale for the restriction in the prior Office Action.

The regulations governing restriction requirements in national stage applications are set forth under 37 C.F.R. §s 1.475 and 1.499 and Rule 13.2 of the Patent Cooperation Treaty. The first section clearly stipulates that unity of invention exists when "there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art." The circumstances in which the Unity of Invention criteria are considered to be met are governed by Rule 13.2 of the Patent Cooperation Treaty which stipulates that "Where a group of inventions is

claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding technical features." In the instant case, the common technical feature of "antigen-specific VLA-1+ T cells in a sample" is not a contribution over the prior art as set forth below in the prior Office Action, and thus, the common technical feature is not a special technical feature. Therefore, the claimed invention cannot be said to have unity of invention.

Additional instructions pertaining to the presentation of alternative chemical or non-chemical species is provided in M.P.E.P. § 1850 [R-7] subsection III. B: "[N]o problem arises in the case of a genus/species situation where the genus claim avoids the prior art, provided the genus claim is directed only to alternatives of a similar nature and the species falls entirely within the genus." In the special situation involving the so-called Markush practice wherein a single claim defines alternatives (chemical or non-chemical), the requirement of a technical interrelationship and the same or corresponding special technical features as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of a similar nature and where the following criteria are fulfilled: (A) All alternatives have a common property or activity; and (B)(1) A common structure is present (i.e., a significant structural element is shared by all of the alternatives); or (B)(2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains. The M.P.E.P. further defines "recognized class of chemical compounds" to mean that "there is an expectation from the knowledge in the

art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved."

Contrary to applicants' arguments, the claimed invention does not meet the requirements concerning unity of invention as set forth in the office action mailed 07 August 2009. The inventions claimed do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. Each combination of subject, tissue sample, antigen, and detection technique is directed toward an independent and distinct invention, each of which will require a separate search, and therefore fail to contain a common special technical feature. For instance, each of the identified antigens is directed toward a different organism and does not share any common structure with another or belong to the same recognized class of chemical compounds. Each of these antigens has different genotypic and phenotypic properties and will require separate searches. The species of flow cytometry is distinct from the species of positive tetramer staining because flow cytometry is not exclusively used for positive tetramer staining and vice versa. Each species will require a non-coextensive search.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-15, 17, 18, 21-27, 29, 31, 35 and 37-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08 February 2010.

Claims 1-4, 16, 19, 20, 28, 30, 32-34 and 36 are currently examined.

Information Disclosure Statement

Applicant's Information Disclosure Statements (IDS) filed 22 December 2008 has been received and entered into the application. As reflected by the attached, signed and initialed copy of form PTO-1449A (five pages total), the Examiner has considered the cited references.

Specification

The disclosure is objected to because of the following minor informalities:

(i) the acronym "VLA-1" is not defined at the first occurrence on page 1 at line 12; and

(ii) the word "blood" is misspelled at page 6, line 12;

Appropriate correction is required.

Claim Objections

Claim 1 is objected to for failing to define the acronym "VLA-1" at the first occurrence in the claims. Applicant may consider amending the claims to read ---very late antigen-1--- at line 5 of the claim for clarity.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 16, 19, 20, 28, 30, 32-34 and 36 are rejected under 35 U.S.C. §103(a) as being unpatentable over Braun *et al.* (2003; hereinafter "Braun") in view of Novak *et al.* (1999; hereinafter "Novak").

The instant claims are directed to a method of assessing the efficacy of an immune response to a selected antigen in a subject comprising: (1) introducing into the subject the antigen; (2) collecting a tissue sample from the subject; and (3) detecting, or isolating, the presence of and quantifying, or measuring, the level of VLA-1$^+$ antigen-specifiec T cells in the sample. Claims 2-4 further limit the antigen to a viral antigen, and more specifically, an influenza A antigen. Claim 16 further limits the tissue sample to pulmonary lavage, which reads on bronchoalveolar lavage. Claim 19 further limits he antigen-specific T cells to peripheral memory T cells. Claim 20 further limits the collecting step to take place 6-10 days after the antigen introduction. Claim 28 further limits the subject to a human. Claim 30 further limits the detecting step to the technique of flow cytometry. Claim 32 further limits the method to detecting CD45RO, CD45RA, CD44, CD62L, CD27, and CD43 on the VLA-1$^+$ antigen-specific T cells.

Braun discloses a method of assessing the activity and analyzing surface receptor expression of CD4$^+$ T cells from patients (human subjects) with pulmonary diseases (page 20, left column, middle paragraph), comprising the claimed method steps of (2) collecting from the subjects a tissue sample that is bronchoalveolar lavage and (3) detecting and quantifying the level of VLA-1$^+$ T cells (page 24, Table 5) and detecting

activation markers (page 24, Fig. 2) such as CD45RO, CD62L and CD27 by flow cytometry (page 21, right column, first paragraph). CD45RO is a marker for periphery memory T cells (page 20, left column, middle paragraph). Elevated level of VLA-1 is expressed on $CD103^+/CD4^+$ T cells (Abstract), which level is significantly higher in pulmonary diseases than healthy controls (page 19, left column, last four lines). VLA-1 can be detected weeks after activation (page 19, right column), which reads on the claim limitation of wherein the tissue sample is collected 6-10 days after the antigen introduction.

Braun does not disclose introducing an antigen into the subject before detecting, isolating and measuring the VLA-1^+ antigen-specific T cells.

Novak suggests introducing an influenza A virus antigen into human subjects, collecting a tissue sample and detecting antigen-specific T cells by tetramer staining (page R64, right column, last paragraph) and flow cytometry (page R64, Figure 1b).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Braun's immunity assessment method so as to include the initial step of introducing an influenza A antigen, as suggested by Novak. The skilled artisan would have been motivated to make this modification in order to assess the immune response to any antigen introduced to a subject. There would be a reasonable expectation of success because an influenza A virus infects human lungs and the method of how to assess an immune response in human lungs is already disclosed by Braun. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the application as filed so as not to add new matter. See MPEP §714.02 and §2163.06.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louise Humphrey/

Examiner, Art Unit 1648